REMARKS/ARGUMENTS

Claims 1, 2, 4-8, 13-16 and 18 are pending in the current application. Claims 14 and 18 are canceled herein. Claims 1, 2, 4-8, 13-16 and 18 have been examined and were rejected.

Claims 1-2, 5-6, 8 and 13 are amended herein. These amendments are supported by the Specification, drawings and claims as originally filed as described in more detail below; no new matter has been added.

Claims 20-45 are newly presented. These claims are supported by the Specification, drawings and claims as originally filed; no new matter has been added. Support for claims 20-21 can be found in the Specification at e.g., page 9, lines 30-36. Support for claim 22 can be found in the Specification at e.g., page 10, line 9 to page 11, line 1. Support for the recitation of % homology in claims 23 and 24 is found in the Specification at e.g., page 23, lines 2-9. Support for claim 44 is found in the Specification at e.g., page 1, lines 6-12; page 8, lines 19-36; page 12, line 10 to page 13, line 8 and page 59, lines 23-33. Support for the recitation of a naturally occurring sequence in claim 44 is found in the Specification at e.g., page 12, lines 19-21. Support for a pharmaceutically acceptable carrier recited in claim 45 is found in the Specification at e.g., page 20, lines 3-12.

Amendments to the Drawings:

Four replacement Drawing Sheets are submitted herewith.

The first attached replacement drawing sheet (Figs. 12A- 12D) has been amended to conform to 37 C.F.R. 1.84(u) (l) standards for the numbering system for partial views

The second attached replacement drawing sheet (Figs. 13A-13B) has been amended to conform to 37 C.F.R. 1.84(u) (l) standards for the numbering system for partial views

The third attached replacement drawing sheet (Figs. 19A-19D) has been amended to conform to 37 C.F.R. 1.84(u) (l) standards for the numbering system for partial views

The fourth attached replacement drawing sheet (Figs. 25A-25F) has been amended to conform to 37 C.F.R. 1.84(u) (l) standards for the numbering system for partial views

Attachment: Replacement Sheet

SUBSTITUTE SEQUENCE LISTING

Please replace the substitute sequence listing and disk filed on February 20, 2004 with the enclosed third substitute sequence listing in paper and computer readable format. In order to comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, Applicants submitted the first paper copy and computer readable format (CRF) of the Sequence Listing, comprising 60 sequences, on March 18, 2002. A substitute sequence listing comprising 99 sequences was filed February 20, 2004 to include sequences presented on pages 7 and 10 of the Specification that were inadvertently omitted from the original sequence listing. The third substitute sequence listing, submitted herewith, comprises 102 sequences and properly presents each of the sequences presented in the Specification as filed with a unique sequence identifier (SEQ ID NO).

This paper is accompanied by a computer disc containing the second substitute sequence listing in computer readable format (CRF), and a paper copy of the sequence information which has been printed from the CRF sequence listing. The information contained in the second substitute sequence was prepared through the use of the software program "PatentIn version 3.1" and is identical to that of the paper copy. This amendment contains no new matter. Accordingly, entry of this amendment is respectfully requested.

SEQUENCE COMPLIANCE

The Examiner has indicated that the "application fails to comply with the requirements for of 37 CFR § 1.821 through 1.825. Specifically, no sequence listing has been provided which includes the amino acid sequence presented in claim 1 of the instant specification." (3/16/04 Office Action, at page 2). Claim 1 has been amended to obviate this objection. The sequence listing in amended claim 1 (identified by the sequence identifier SEQ ID NO: 64) is in fact in the sequence listing and the CRF (see 2/20/04 substitute sequence listing at page 25; and the 2/20/04 Amendment at pages 2 and 6, directing entry of the substitute sequence listing).

DRAWINGS

As requested by the Examiner on page 3 of the 3/16/04 Office Action, Figures 12, 13, 19 and 25 have been amended (see the Amendments to the Drawings section, above). Replacement drawing sheets are submitted herewith. Also, as requested by the Examiner, the Specification has been amended to reflect the changes in the Figures.

SPECIFICATION

As requested by the Examiner, the Specification has been amended to delete the embedded hyperlinks (see Amendments to the Specification section, above). Also the Specification has been amended to provide the clarification the Examiner request ed at page 4 of the current Office Action.

The Examiner indicates that the amendment submitted on January 29, 2004 provided the wrong page numbers for replacement paragraphs at page 7, line 27. (See 3/16/04 Office Action, at page 4). Applicants respectfully submit that page 7 is indeed the correct page number for the replacement paragraph beginning "Further, the present invention demonstrated that addition of a FLAG tag." (See the Specification at page 7, line 27).

OBJECTIONS

Claims 5-8, 13-16 were objected to under "37 CFR § 1.75 (c) as being of improper dependent form for failing to further limit the subject matter of a previous claim." (3/16/04 Office Action, at page 4). Claim 5 has been amended to obviate this objection.

REJECTION UNDER 35 U.S.C. § 101

Claims 1, 2, 5 and 18 were rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. (See 3/16/04 Office Action, at page 5). Specifically, the Examiner has contended that "[t]he claims fail to include any limitations which would distinguish the claimed polypeptides and DNA from those which occur in nature." *Id.* Without acquiescing to the rejection, applicants have amended claims 1, 2 and 5 to overcome the rejection. These

claims now recite an "isolated polypeptide." Applicants submit that the term "isolated" distinguishes over a product of nature. Also, claim 18 has been cancelled so the rejection is now moot with regard to this claim. Accordingly, withdrawal of the rejection is respectfully requested.

ENABLEMENT REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶ 0F CLAIMS 2, 4-8, 13-16

Claims 2, 4-8 and 13-16 were rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the claims fail to meet the enablement requirement of 35 U.S.C. §112, first paragraph. (See 3/16/04 Office Action, at page 5). Specifically, the Examiner has contended that the Specification fails to provide any guidance for the skilled artisan how to make a polypeptide encompassed by claim 2, thereby requiring undue experimentation to discover how to use Applicants invention as currently claimed. (See 3/16/04 Office Action, at page 6). The Examiner further contends that the "specification is not found to be enabling for a polypeptide of SEQ ID NO: 5, wherein one or more amino acids have been substituted, deleted, inserted and/or added, such polypeptide [sic]suppresses neuronal death associated with Alzheimer's disease." (See 3/16/04 Office Action, at page7).

Applicants respectfully traverse the above rejection. Contrary to the Examiner's assertions, the Specification provides extensive teaching on how to make polypeptides of SEQ ID NO: 5 which suppress neuronal death associated with Alzheimer's disease wherein one or more amino acids have been substituted, deleted, inserted and/or added. See, for example, Example 6 of the Specification, which describes that a polypeptide in which the C-terminal KRRA has been replaced with AAAA (SEQ ID NO: 10) shows similar functional activity to the original polypeptide (See the Specification at pages 48 to 49). Also, Example 15 describes a variant of SEQ ID NO: 5 that shows an activity of suppressing neuronal death that is even more potent than SEQ ID NO: 5 (See the Specification at pages 59-60). Additionally, Example 13 demonstrates that seven amino acids can be deleted from SEQ ID NO: 5 without loss of function (SEQ ID NO: 21). Further, Figure 23 shows that ten positions of the amino acid sequence of HNG17, a variant consisting of 17 amino acids (SEQ ID NO: 24), can be substituted without loss

of function. Other examples in the Specification of variants of SEQ ID NO: 5 that suppress neuronal death include SEQ ID NOs: 8, 12, 13, 22, 23, 26 -29, 32, 33, 37, 40, 46, 48, 54, and 60. (Applicants also note a paper by, Carocasole *et al.* (FASEB J., 2002, 16: 1331-133, attached) who report a rat homolog of the polypeptide of SEQ ID NO: 5 which has an amino acid sequence in which six amino acids in SEQ ID NO: 5 are substituted (Fig. 1A of Carocasole *et al.*). This polypeptide shows neuroprotective activity as the polypeptide of SEQ ID NO: 5 (Fig. 1B and C))

Moreover, the Specification as filed describes techniques for making variants of the claimed polypeptides (See e.g., page 7, line 10 to page 11, line 1) as well as assays for determining the neural protective activity of those variants (See the Specification e.g., at page 11, line 2 to page 12, line 1; and Examples 1-15). Thus, given this disclosure, the skilled artisan would have been readily able to make and use polypeptide variants of the amino acid sequence of SEQ ID NO:5 having neural protective activity without undue experimentation using techniques described in the Specification and known in the art. However, to expedite prosecution and without acquiescing to the Examiner's rejection, Applicants have amended claim 2 to now recite "a polypeptide that suppresses neuronal death associated with Alzheimer's disease having an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60, wherein one to five amino acids have been substituted, deleted, inserted, and/or added." Specific support for variants of SEQ ID NO: 5 that suppress neuronal death associated with Alzheimer's disease wherein one to five amino acids have been substituted, deleted, inserted, and/or added may be found in the Specification at e.g., page 12, lines 10-21. Also, support for clause c may be found in the Specification e.g., at page 12, line 22 to page 13, line 8.

In light of the above discussion, Applicants submit there is more than ample support in Specification for making and using polypeptides of SEQ ID NO: 5 that suppress neuronal death associated with Alzheimer's disease, wherein one to five amino acids have been substituted, deleted, inserted, and/or added. Accordingly, withdrawal of the rejection is respectfully requested.

ENABLEMENT REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶ 0F CLAIMS 13-16

Claims 13-16 were rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the claims fail to meet the enablement requirement of 35 U.S.C. §112, first paragraph. (See 3/16/04 Office Action, at page 9). The Examiner would appear to contend that the Specification does not provide sufficient teaching for the skilled artisan to use the claimed polypeptides and/or polynucleotides to treat Alzheimer's disease in a human because, *inter alia*, in vitro data cannot be used to support enablement of pharmaceutical composition claims and because the Specification has not provided information on the route, duration and quantity of administration of the claimed pharmaceutical composition. (See 3/16/04 Office Action, at pages 10-11). Applicants respectfully traverse this rejection. Each of the Examiner's contentions will be addressed in turn.

In regard to the use of in vitro data, the courts have ruled that in vitro data can be used to support enablement of pharmaceutical inventions. *Cross v.Izuka,* 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985). Moreover, a rigorous or exact correlation between in vitro and in vivo activity is not required where "the disclosure of the pharmaceutical activity if reasonably based on the probative evidence." *Id.*

The Specification establishes a correlation between the in vitro and in vivo activity of the claimed polypeptides. In particular, the Specification teaches that the claimed polypeptides produced a dramatic neuroprotective effect for primary neurons exposed to Aβ 1-43 peptide (See the Specification at page 52, line 11 to page 53, line 5). Aβ 1-43 peptide is a type of beta-amyloid protein (Aß). The links between Aβ and Alzheimer's disease are well established in that Aß is the major peptide component of senile plaque in humans and an extracellular deposit that pathologically characterizes an Alzheimer's diseased brain. Also, it is suggested to be associated with the pathological mechanism of Alzheimer's disease (AD). (See the Specification at page 51, line 35 to page 52, line 2).

Importantly, the neuroprotectve effect conferred by claimed polypeptides was selective, i.e., no such effect was produced when primary neurons were exposed to Etoposide, an anticancer agent and has been reported to induce cell death of primary cultured neurons (See the

Specification at page 51, lines 21-29). Therefore, by conferring a selective in vitro neuroprotective effect against Aβ 1-43 (a compound associated with the in vivo pathological mechanism of AD), the claimed polypeptides would be reasonably expected to do so in vivo in a human, thus satisfying the enablement requirements of *Cross*. Further support for an expected in vivo effect is seen in the fact that the claimed polypeptides also produced a neuroprotective effect for cells expressing neurodegenerative disease-causing FAD (familial Alzheimer's disease) genes (See Examples 7-9 of Specification).

Additional support of an in vivo therapeutic effect of the claimed polypeptides is evidenced by the papers of Hashimoto et al. (Proc Natl. Acad. Sci. U S A. 2001 May 22; 98 (11): 6336–634) and Mamiya et al. (British J. Pharmacol. 2001, 134: 1597-1599), copies of which are attached. Hashimoto et al. demonstrated that the claimed peptides confer a neuroprotective effect to cells expressing Alzheimer's disease-linked genes but not Huntington's disease or amyotrophic lateral sclerosis-linked genes. This result again suggests that the neuroprotective effect of the claimed peptides is highly specific and that they are likely to provide a therapeutic benefit.

Mamiya et al. report the in vivo effects of the polypeptide of SEQ ID NO: 8 (S14G substitution of SEQ ID NO: 5). This paper teaches that cholinergic neuronal systems play an important role in the cognitive deficits associated with neurodegenerative diseases including AD, and that scopolamine antagonizes a muscarinic acetylcholine receptor, thereby inducing impairment of learning and memory (See page 1598, right column, "Discussion"). Figure 1 and Table 1 of Mamiya et al. demonstrate that intracerebroventricular (i.c.v.) administration to mice of the polypeptide of SEQ ID NO: 8 exerts the anti-amnesic effects on learning and memory deficits induced by scopolamine.

Contrary to the Examiner's second basis for rejection (e.g.,. alleged lack of teaching on administration etc.), the Specification provides extensive teaching on the route, duration and quantity of administration of the claimed polypeptides for use in a pharmaceutical composition. For example at page 20, lines 1-30, the Specification provides teaching on the formulation, route and methods of administration of the claimed polypeptides. Further, at page 20 line 23 to page 21, line,12 the Specification provides teaching on the concentration and dosage of the claimed

polypeptides in a pharmaceutical composition. Applicants respectfully submit that this is more than sufficient teaching of the parameters the Examiner alludes to in the Office Action.

For all the reasons above, Applicants submit the pharmaceutical composition of claim 13 is enabled and therefore, respectfully request withdrawal of the rejection.

ENABLEMENT REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶ 0F CLAIM 8

Claim 8 was rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the claim fails to meet the enablement requirement of 35 U.S.C. §112, first paragraph. (See 3/16/04 Office Action at page 12). Specifically the Examiner contends that the Specification does not provide any guidance or working examples to teach one skilled in the art on how to practice a method for producing the polypeptide of any one of claims 1 to 2 by using DNA encoding a fusion polypeptide comprising the polypeptide of any one of claims 1 to 2 fused with one or more other polypeptides. (See 3/16/04 Office Action, at page 13)

Applicants respectfully traverse this rejection. Contrary to the Examiner's assertions, the Specification provides extensive teaching on fusion polypeptides and related production methods (See the Specification at e.g., page 14, lines 2-19). Also, the Examiner correctly acknowledges that the Specification is enabling for a method for producing the polypeptide of any one of claims 1 to 2 comprising culturing a host cell retaining a vector into which a DNA encoding the polypeptide of any one of claims 1 to 2 is inserted and recovering an expressed polypeptide from the host cell or culture supernatant thereof. (See 3/16/04 Office Action at page 12). Thus, Applicants submit that the claimed fusion polypeptides could be produced by the same host cell culturing methods as the polypeptides of any one of claims 1 to 2. Accordingly, on this basis, Applicants respectfully request withdrawal of the rejection.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). Applicants submit that fusion polypeptides and their production using host cells retaining a vector into which a DNA encoding the fusion polypeptide is inserted are indeed well known in the art. Thus, Applicants further submit that given the disclosure in the

Specification, as well as the teachings in the art, it would have been routine for one skilled in the art to use the method of claim 8 for producing the claimed fusion polypeptides and no undue experimentation would be required.

Also, the rejection is legally insufficient in that it fails to meet the requirements for non-enablement set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 ***requires nothing more than objective enablement***. [Emphasis added] How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

However, contrary to the standard set forth in *Marzocchi*, the Examiner has failed to provide any reasons that one would doubt that the guidance provided by the Specification would enable one to make the claimed fusion polypeptides using the method of claim 8. On the contrary, the Examiner actually affirms the enablement of method claim 8 by acknowledging that this method is enabling for producing the polypeptides of claims 1 and 2. Hence, a prima facie case for non-enablement has not been established with respect to producing the claimed fusion polypeptides using the method of claim 8. Accordingly for this separate and additional reason, withdrawal of this rejection is respectfully requested.

WRITTEN DESCRIPTION REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶

Claims 2, 4-8, 13-16 and 18 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. (See 3/16/04 Office Action, at page 7). In particular, the Examiner bases her rejection on the contention that the Specification "fails to teach or describe any other proteins [besides the amino acid sequence of SEQ ID NO:5] which has one or more amino acids substituted, deleted, inserted and/or added and has activities recited as 'suppresses neuronal death associated with Alzheimer's disease.'" (3/16/04 Office Action, at page 8). The Examiner also bases her rejection on the contention that the Specification, does not describe structural features which distinguish the genus from others in the protein class, and that the Specification does not disclose a representative number of species to describe the genus. (See 3/16/04 Office Action, at pages 7-9). Each of these issues will be addressed in turn.

First, the Examiner contends that the Specification "fails to teach or describe any other proteins [besides the amino acid sequence of SEQ ID NO:5] which has one or more amino acids substituted, deleted, inserted and/or added and has activities recited as 'suppresses neuronal death associated with Alzheimer's disease.'" (3/16/04 Office Action, at page 8) Such is not the case, the Specification provides extensive disclosure of polypeptides of SEQ ID NO: 5 which suppress neuronal death associated with Alzheimer's disease wherein one or more amino acids have been substituted, deleted, inserted and/or added. See, for example, Example 6 of the Specification which describes that a polypeptide in which the C-terminal KRRA has been replaced with AAAA (SEQ ID NO: 10), shows similar functional activity to the original polypeptide (See the Specification at pages 48 to 49). Also, Example 15 describes a variant of SEQ ID NO: 5 that shows an activity of suppressing neuronal death that is even more potent than SEQ ID NO: 5 (See the Specification at pages 59-60). Additionally, Example 13 demonstrates that seven amino acids can be deleted from SEQ ID NO: 5 without loss of function (SEQ ID NO: 21). Further, Figure 23 shows that ten positions of the amino acid sequence of HNG17, a variant

consisting of 17 amino acids (SEQ ID NO: 24), can be substituted without loss of function. Other examples disclosed in the Specification of variants of SEQ ID NO: 5 that suppress neuronal death include SEQ ID NOs: 8, 12, 13, 22, 23, 26 -29, 32, 33, 37, 40, 46, 48, 54, and 60.

The Examiner also bases her rejection on the contention that the Specification does not describe structural features which distinguish the genus from others in the protein class. (See 3/16/04 Office Action, at page 9) However, the Specification in fact discloses the complete structure of a number of species in the genus including the polypeptides of SEQ ID NOs: 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54 and 60. (See the Sequence listing which discloses the complete structure of each of these polypeptides).

Next the Office Action contends that the Specification fails to provide a representative number of species to describe the claimed genus (those proteins with one or more amino acids substituted, deleted, inserted and/or added which suppress neuronal death associated with Alzheimer's disease). (See 3/16/04 Office Action, at pages 9) Applicants submit that the list of 22 polypeptides described in the preceding paragraph which suppress neuronal death associated with Alzheimer's disease is a representative number of species for the "claimed genus (those proteins with one or more amino acids substituted, deleted, inserted and/or added, such proteins suppress neuronal death associated with Alzheimer's disease)."

The Examiner also bases her rejection on the contention that "specification fails to describe the entire genus of proteins, which are encompassed by these claims." However, such a disclosure is not required for an adequate written description. The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. [footnotes omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art. Applicants submit that the subject matter encompassed by claims 2, 4-8, 13-16 and 18 is fulfilled by what is disclosed in the Specification. As described above, the Specification provides extensive disclosure of polypeptides of SEQ ID NO: 5 which suppress neuronal death associated with Alzheimer's disease wherein one or more amino acids have been substituted, deleted, inserted and/or added. In particular, the Specification provides specific disclosure of numerous species in this genus including the polypeptides of SEQ ID NOs: 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54 and 60. Accordingly, Applicants submit that Specification has more than satisfied the written description requirement for the subject matter encompassed by claims 2, 4-8, 13-16 and 18.

However, in order to expedite prosecution, and without acquiescing to the Examiner's rejection, Applicants have amended claim 2 to now recite "a polypeptide that suppresses neuronal death associated with Alzheimer's disease having an amino acid sequence selected

from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60, wherein one to five amino acids have been substituted, deleted, inserted, and/or added." Specific written description for variants of SEQ ID NO: 5 that suppress neuronal death associated with Alzheimer's disease wherein one to five amino acids have been substituted, deleted, inserted, and/or added may be found in the Specification at e.g., page 12, lines 10-21. Also Applicants have cancelled claim 18, thus mooting the rejection in regard to this claim.

In light of the above discussion and amendments, Applicants submit that claims 2, 4-8, 13-16 are now allowable. Accordingly, withdrawal of the rejection is respectfully requested.

INDEFINITENESS REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 8, 13-16 and 18 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. (See 3/16/04 Office Action, at page 13). Without acquiescing to the propriety of the rejection, Applicants have amended claims 8 and 13 to obviate the rejection. Also, claim 18 has been cancelled thus mooting, the rejection with regard to this claim. Accordingly, withdrawal of the rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. § 102

Claim 18 has been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by publication NCI CGAP, Genbank Accession No. AA579497, 1997. (3/16/04 Office Action, at page 14) Without acquiescing to the rejection, Applicants have cancelled claim 18, thus mooting the rejection.

DOUBLE PATENTING

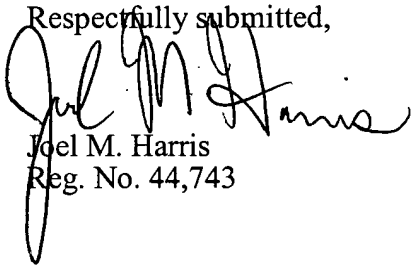
The Examiner has indicated that "should claim 13 be allowable claim 14 will be objected to under 37 CFR § 1.75 as being a substantial duplicate thereof." (3/16/04 Office Action, at page 14) Applicants have cancelled claim 14, thus mooting this potential objection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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